PATENT COOPERATION TREATY

TRANSLATION

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

	Date of mailing *(day/month/year)*
Applicant's or agent's file reference **FP2630PCT**	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/JP2004/002124	24.02.2004	

International Patent Classification (IPC) or both national classification and IPC

Applicant
TTC CO., LTD.

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☐ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☐ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/JP	Authorized officer
Facsimile No.	Telephone No.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
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Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:

   ☐ paid additional fees

   ☐ paid additional fees under protest

   ☐ not paid additional fees

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

The inventions described in claims 1-3 and the invention described in claim 4 have a common matter of relating to BL angiostatin, but because BL angiostatin is publicly known, as described in [JP 2002-272453 A], no technical relationship between these inventions involving one or more of the same of corresponding special technical features is considered to be present.

Thus, this international application is not considered to satisfy the requirement of unity of invention.

4. Consequently, this opinion has been established in respect of the following parts of the international application:

   ☒ all parts

   ☐ the parts relating to claims Nos. _____

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

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Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	4	YES
	Claims	1-3	NO
Inventive step (IS)	Claims		YES
	Claims	1-4	NO
Industrial applicability (IA)	Claims	1-4	YES
	Claims		NO

2. Citations and explanations:

Document 1. JP 2002-272453 A (Japan Science and Technology Corporation)
Document 2. SHIMIZU, Kousuke et al, Japan Society for Bioscience, Biotechnology, and Agrochemistry, 2003, Vol. 2003, page 258
Document 3. JP 9-286798 A (Juridical Foundation The Chemo-Sero-Therapeutic Research Institute)
Document 4. WO 96/35774 A2 (The Children's Medical Center Corporation)
Document 5. WO 98/54217 A2 (The Children's Medical Center Corporation)

Document 1 describes the possible use of BL angiostatin as an angiogenesis suppressor and the possible use of an angiogenesis suppressor in the treatment of cancer. In addition, the possible use of angiostatin substances analogous to BL angiostatin in the treatment of cancer is well known, as described in documents 2-5. Document 1 also describes BL angiostatin as a matter selected from a group comprising human plasminogen Glu^{1}-Ser^{441}, Glu^{1}-Val^{499}, Phe^{75}-Ser^{441}, and Phe^{75}-Val^{449} fragments.

The inventions described in claims 1-3 do not appear to possess novelty or involve an inventive step.

Document 2 describes adding plasma to an affinity trap reactor wherein bacillolysin MA and lysine immobilized on a carrier and supplementing plasminogen, then eluting BL angiostatin using a lysine analog. 6-aminohexanoic acid is well-known as an eluate for plasminogen lysine bound fragments, as described in documents 3-5 (examples in document 3, page 71 line 21 in document 4, and page 87 line 1 in document 5), so the selection of 6-aminohexanoic acid as a lysine analog in document 2 would be a matter obvious to a specialist in the relevant technical field.

No exceptional results are considered to be produced by the inventions described in the claims.

The invention described in claim 4 does not appear to involve an inventive step.

The inventions described in claims 1-4 appear to possess industrial applicability.